REMARKS

Claims 1-11, 14, 15, 26-42 and 57 are pending in the application.

Claims 6, 9, 14, 26-42 and 57 have been withdrawn from consideration as being drawn to non-elected species (ribosome display and phage display).

Claims 1-5, 7, 8, 10, 11, and 15 have been amended. In light of these amendments and the following traverse reconsideration and allowance of all claims is respectfully requested.

I. Preliminary Matters.

The Examiner withdrew claims 6, 9, 14, 26 and 57 from further consideration as being drawn to non-elected species. Applicant hereby withdraws claims 27-42 from further consideration, since these claims are also drawn to the non-elected species of ribosome display and phage display.

II. Amended Claims.

Claim 1 has been amended to more clearly set forth the steps of the screening method and to address 35 U.S.C. §112 issues raised in the Office Action. Claim 1 is directed to a four step method for screening proteins and polypeptides to identify a protein or polypeptide having a biological activity of interest. The method comprises the sequential steps of (i) forming a first library of polynucleotide clones, (ii) expressing individual proteins or polypeptides from each of the clones in the first library to form a second library of proteins and polypeptides, (iii) assaying the second library to select a protein or polypeptide having a biological activity of interest, and (iv) identifying the protein or polypeptide selected in step (iii) by sequencing the polynucleotide from the first library that encodes the selected protein or polypeptide. Support for these amendments are found in the specification starting on page 3 line 8, through page 5, line 24, page 10, line 1, through page 12, line 3, and Examples 3-7 on pages 54-60.

Claim 2 has been amended to address 35 U.S.C. §112 issues raised in the Office Action and to conform the language of this claim to claim 1, from which it depends. The alternative language of the claim has been replaced with a standard Markush group. Support for the amendment is found in original claim 2 and on page 33, lines 14-29 of the

specification.

Claim 3 has been amended to address 35 U.S.C. §112 issues raised in the Office Action. Support for this amendment is found in original claim 3.

Claim 4 has been amended to address 35 U.S.C. §112 issues raised in the Office Action and to conform the language of this claim to claim 1, from which it depends. Support for this amendment is found in original claim 4 and on page 11, lines 13-20 of the specification.

Claim 5 has been amended to conform the language of this claim to claim 1, from which it depends. Support for this amendment is found in original claim 5.

Claim 7 has been amended to address 35 U.S.C. §112 issues raised in the Office Action and to conform the language of this claim to claim 1, from which it depends. Support for the amendment is found in original claim 7.

Claim 8 has been amended to conform the language of the claim to claim 1, from which it depends. Support for the amendment is found in original claim 8.

Claim 10 has been amended to address 35 U.S.C. §112 issues raised in the Office Action and to conform the language of this claim to claim 1, from which it depends. Support for this amendment is found in original claim 10 and on page 13, lines 1-14.

Claim 11 has been amended to conform the language of this claim to claim 1, from which it depends. Support for this amendment is found in original claim 11.

Claim 15 has been amended to address 35 U.S.C. §112 issues raised in the Office Action. Support for this amendment is found in original claim 15 and in the specification on page 9, line 28, through page 11, line 11.

The present amendments do not add new matter to the application.

III. Claims 1-5, 7-8, 10-11, and 15 are not indefinite.

Claims 1-5, 7-8, 10-11, and 15 stand rejected under 35 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter that the Applicant regards as the invention. The various grounds for the rejections are set forth in lettered paragraphs A through V on pages 5-11 of the Office Action. Claims 27-42 have been withdrawn as being directed to non-elected species. The claims that are currently

under consideration have been amended to address the issues raised in the Office Action. Applicant shall address each ground for rejection in turn.

A. Claims 1-2 were rejected as vague and indefinite for using the verb "can" and for lack of clarity as to whether a screening method is described. The claims have been amended to distinctly set forth steps of a screening method without the use of "can."

B. Claim 1 was deemed vague in that it was not clear what can be screened and whether the proteins are related to the gene library. The claim has been amended to recite a method of screening proteins and polypeptides to identify a biological activity thereof. The proteins and polypeptides to be screened are expressed from the polynucleotide library.

C. Claims 1, 3, 4, 7, and 15 were rejected because the use of the term "gene library" was deemed vague and indefinite. The claims have been amended to replace "gene" with "polynucleotide" as suggested by the Examiner to overcome this rejection.

D. Claim 1 was deemed unclear regarding whether the "synthesized individual proteins" are derived from the "gene" library. The claim has been amended to specify that a protein and polypeptide library is generated from the polynucleotide library.

E. The term "derived from" in claim 3 was deemed vague and indefinite as to how the gene library is derived from the mRNA library. The phrase "derived from" in the original claim was meant as a designation of identity, not a functional limitation. The claim has been amended to delete "derived from" and to recite that the library is a library of mRNA from a cell or tissue.

F. The phase "such as" in claims 4 and 10 were deemed to render the claims indefinite. The claims have been amended to delete the phrase "such as."

G. In claim 4, the term "library of variable molecules" was deemed vague and indefinite. The claim has been amended to state that the library of proteins and polypeptides comprises fragments of antibody variable regions, and the term "library of variable molecules" has been deleted.

H. Claim 10 was rejected because the phrase "wherein the solid phase is a continuous surface" was deemed vague and indefinite." Claim 10 has been amended to specify that the solid phase is a glass plate and the phrase "continuous surface" has been deleted.

I. Claim 15 was rejected because there was insufficient antecedent basis for the limitation "nucleic acid." The claim has been amended to replace this limitation with "polynucleotide" for which there is now antecedent basis in the claim.

J. Claim 15 was rejected because there was insufficient antecedent basis for the limitation "each clone." The claim has been amended to specify that the polynucleotide library consists of specified types of clones, which provides the required antecedent basis for "each clone."

Lettered paragraphs K-V rejected claims 27-31 and 33-41 for a variety of reasons under the second paragraph of 35 U.S.C. §112. Since claims 27-31 and 33-41 have been withdrawn from further consideration, these grounds for rejection are now moot.

The present amendments to claims 1-4, 7, 10 and 15 have addressed and corrected all of the 35 U.S.C. §112 issues under which the presently pending claims were rejected. Withdrawal of all rejections under the second paragraph of 35 U.S.C. §112 is respectfully requested.

IV. Claims 1-5, 7-8, 10-11, and 15 are not anticipated by Johnstone *et al.*

Claim 1-5, 7, 8, 10, 11, and 15 stand rejected under 35 U.S.C. §102(b) as being anticipated by Johnstone *et al.* In view of the amendments and traverse presented herein, Applicant requests that this ground for rejection be withdrawn.

Claim 1, and claims 2-5, 7, 8, 10, and 11, which depend therefrom, are all directed to methods of screening proteins and polypeptides involving the sequential steps of (i) forming a first library of polynucleotides, (ii) expressing proteins and polypeptides from the polynucleotide library to form a second library of individual proteins and polypeptides therefrom, (iii) assaying the second library to select an individual protein or polypeptide having a biological activity of interest, and (iv) identifying the selected protein or polypeptide by sequencing the polynucleotide from the first library that encodes the protein or polypeptide selected in the step (iii). As described on page 10, line 1, through page 12, line 3, this screening method provides a way of rapidly identifying proteins and polypeptides that are associated with a disease state or with individual genetic variability, and provides a way of assessing difference in gene expression from various cell and tissue types. The method also

avoids the use of gel electrophoresis.

As pointed out on page 12 of the Office Action, Johnstone *et al.* disclose a method for high throughput screening of a large population of host cells (hybridomas) for the production of monoclonal antibodies. Johnstone *et al.* provides a primer for preparing monoclonal antibodies from hybridoma cells. Furthermore, Johnstone *et al.* do not teach or suggest a screening process where a specific protein or polypeptide is selected based on its biological activity, and is identified by sequencing the polynucleotide encoding the protein or polypeptide. The teaching of Johnstone *et al.* is directed to forming monoclonal antibodies, not to *identifying* proteins or polypeptides having a specified biological activity of interest by sequencing the polynucleotide encoding the protein or polypeptide.

Assuming, *arguendo* that the hybridoma cells represent a first polynucleotide library, as asserted in the Office Action, Johnstone *et al.* do not disclose forming a second library of individual proteins and polypeptides from the first library, assaying the second library to select a protein or polypeptide having a biological activity of interest, and *subsequently* identifying the selected protein or polypeptide by sequencing the polynucleotide from the first library that encodes the selected protein or polypeptide from the second library. In Johnstone *et al.* hybridoma cells are assayed for production of monoclonal antibodies; however, the reference does not teach or suggest identifying the antibodies by sequencing the polynucleotides that encode the antibodies.

Claims 1-5, 7, 8, 10, and 11 are directed to methods involving multiple steps in a specified order of performance. Since Johnstone *et al.* do not teach or suggest every step of the claimed methods, in the sequential order required by the claims, this reference cannot anticipate claims 1-5, 7, 8, 10, and 11.

Claim 15 is directed to a method of screening proteins and polypeptides similar to that of claim 1, in which the polynucleotide library is formed from specified clones, the proteins and polypeptides expressed from the clones are distributed in an array, and the biological activity of interest is an interaction of a protein or polypeptide in the array with a cell or tissue. Like claim 1, claim 15 also includes the step of identifying the protein or polypeptide by sequencing the polynucleotide that encodes the selected protein or

polypeptide.

As described above, Johnstone *et al.* do not teach or suggest a method of screening proteins and polypeptides involving the sequential steps recited in the present claims. Furthermore, Johnstone *et al.* do not teach or suggest a screening process where a specific protein or polypeptide is selected and then identified by sequencing the polynucleotide encoding the protein or polypeptide . The teaching of Johnstone *et al.* is directed to forming monoclonal antibodies, not to identifying proteins or polypeptides having a specified biological activity of interest.

Since Johnstone *et al.* do not teach or suggest every step of the claimed method in the sequence specified, this reference cannot anticipate claim 15.

V. Claims 1-5, 7-8, 10-11, and 15 are not anticipated by Ghai *et al.*

Claim 1-5, 7, 8, 10, 11, and 15 stand rejected under 35 U.S.C. §102(e) as being anticipated by Ghai *et al.* In view of the amendments and traverse presented herein, Applicant requests that this ground for rejection also be withdrawn.

As noted above, claim 1-5, 7, 8, 10, 11, and 15 are all directed to methods of screening proteins and polypeptides involving four sequential steps of forming a first library of polynucleotides, expressing the polynucleotides to form a second library of proteins and polypeptides, assaying the second library to select a protein or polypeptide having a biological activity of interest, and identifying the selected protein or polypeptide by sequencing the polynucleotide from the first library that encodes the selected protein or polynucleotide from the second library. The method involves selecting and identifying previously unknown proteins and polypeptides and the polynucleotides (genes) that encode them.

Ghai *et al.* is directed to a method of screening foods for the presence of nutraceuticals. Unlike the presently claimed methods, the method of Ghai *et al.* involves providing cultured cells that include within their genetic makeup a *previously identified gene* that is associated with a specific and known disease state or a specific and known biological activity. See Ghai *et al.*, col. 2, line 50, through col. 3, line 3, and col. 3, line 66 through col. 4, line 32. Various test materials are screened as potential sources of nutraceuticals by exposing the cells to the test materials and observing the effect that the test materials have on

the expression of the identified gene in the cells. An increase or decrease in expression of the gene in the cell after exposure to the test material indicates that the test material is a potential source of an agent for treating the disease associated with the identified gene, for example. The effect of the test material on the gene can be assayed, for example, by observing levels of mRNA or by observing levels of gene products produced by the cells. However, the method of Ghai *et al.* is dependent on having already identified the presence of the specific, known gene in the cells, which in turn has a known biological function. See col. 6, line 64, through col. 7, line 3, and col. 7, lines 53-58.

The method of Ghai *et al.* starts where the present method finishes. The presently claimed methods provide a way of identifying previously unknown proteins and genes having a biological activity of interest. The methods of Ghai *et al.* require that a known gene, with a known function be present in the cells and then looks at the effects of exposure to various test materials on the expression of the known disease to identify a useful medicinal agent (i.e., a nutraceutical). Ghai *et al.* do not teach or suggest a method that starts with a library of different polynucleotides of *unknown* function, creating a second library of proteins and polypeptides from the first library; assaying the second library to select individual proteins and polypeptides having a biological activity of interest, and then identifying the selected protein or polypeptide by sequencing the polynucleotide from the first library that encoded the selected protein or polypeptide.

The applied reference does not anticipate any of the present claims because Ghai *et al.* is directed to a totally different purpose than the present invention and does not teach or suggest all of the limitations of the present method in the order specified by the claims. The purpose of Ghai *et al.* is to identify the effect of various materials on the expression of a *known* gene, while the purpose of the present invention is to identify previously *unknown* or unidentified proteins and polypeptides having a biological activity of interest.

Ghai *et al.* do not teach or suggest all of the elements of the present claims, and the teachings of the reference are inapposite to the teachings and practice of the present invention. Therefore, the reference does not anticipate the present claims and Applicant requests that this ground for rejection be withdrawn.

VI. The Present Claims are Not Obvious Over Ghai *et al.* in View of Wagner.

Claims 1-5, 7, 8, 10, 11, 15, 27-42 stand rejected under 35 U.S.C. §103(a) as being obvious over Ghai *et al.* in view of Wagner (EP 0174753). According to the Office Action, on pages 29-31, Claims 1-5, 7, 8, 10, 11, 15, 27-32, 34-39, and 42 are rendered obvious by Ghai *et al.* alone, since these claims were allegedly anticipated by Ghai *et al.* Wagner is cited to overcome deficiencies in Ghai *et al.* with respect to claims 33, 40, and 41.

For the reasons stated above with respect to anticipation, Claims 1-5, 7, 8, 10, 11, and 15 are not obvious over Ghai *et al.* Since claims 27-42 have been withdrawn, the issue of whether these claims are obvious over Ghai *et al.* in view of Wagner is moot and should be withdrawn.

VII. Conclusion.

Claims 1-5, 7, 8, 10, 11, and 15 are deemed patentable over the applied references and in compliance with 35 U.S.C. §112, second paragraph. Reconsideration and early passing of this application to issue is earnestly solicited.

Respectfully submitted,

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